Prion Diseases

(Also known as Transmissible Spongiform Encephalopathies [TSEs]; includes Creutzfeldt-Jakob disease [CJD], Gerstmann-Straussler-Scheinker Disease [GSS], Fatal Familial Insomnia [FFI], Kuru, and Variant CJD [vCJD])

Section 1:

ABOUT THE DISEASE

A. Etiologic Agent

Prion diseases, also known as transmissible spongiform encephalopathies (TSE), are a group of rare, rapidly progressive, and fatal neurologic diseases. The agents responsible for human and animal prion diseases are thought to be abnormal proteins (protease-resistant prion protein, or PrP-res) that can trigger chain reactions causing normal proteins in the brain to change to the abnormal protein. These abnormal proteins are resistant to enzymatic breakdown, and they accumulate in the brain, leading to damage. There are a number of animal and human prion diseases. Human diseases include Creutzfeldt-Jakob disease (CJD), Gerstmann-Straussler-Scheinker Disease (GSS), fatal familial insomnia (FFI), kuru, and variant CJD (vCJD). CJD has several sub-categories: sporadic (sCJD, accounting for 80–90% of CJD cases); familial (hereditary CJD); iatrogenic (associated with treatment and transplant, such as use of infected dura mater patches or administration of human pituitary-derived hormones); and variant (vCJD, associated with exposure to bovine spongiform encephalopathy [BSE]). Examples of animal prion diseases include scrapie in sheep and goats, chronic wasting disease (CWD) in deer and elk, transmissible mink encephalopathy (TME), feline spongiform encephalopathy, and BSE (also called "mad cow disease").

B. Clinical Description

Prion diseases are characterized by the absence of inflammation, loss of brain tissue in a spongiform pattern, and an unusually long incubation period. CJD symptoms include confusion progressing to dementia, as well as early personality changes and movement disorders including ataxia (lack of muscle coordination) and dysarthria (difficulty in speech). Myoclonus (muscle twitching) and other neurologic symptoms appear late. Fever is not characteristic. The case-fatality rate is 100%, and death usually occurs within 3–12 months (the median is 4 months, the mean is 7 months); approximately 10% of patients with CJD survive for more than 1 year. Variant CJD (vCJD) is distinguished from CJD by a typical younger age of onset, early psychiatric and behavioral symptoms (depression or psychosis), painful sensory symptoms (e.g., "stickiness" of the skin), delayed onset of unsteadiness, difficulty walking and involuntary movements, and a longer clinical course of illness (a mean of 14 months versus 7 months for sporadic CJD).

C. Vectors and Reservoirs

Humans are the only known reservoir for CJD, kuru, GSS, and FFI. The reservoir for vCJD is believed to be BSE-infected cattle.

D. Modes of Transmission

The mode of transmission of sCJD is unknown. It is theorized that sporadic mutations or genetic susceptibility to spontaneous mutations (for familial variants) in the normal protein result in disease. Iatrogenic CJD is acquired following certain medical procedures, such as transplantation of prion-infected corneas or other tissues, the administration of hormones derived from human glands, or by contaminated neurosurgical instruments. Although not firmly established, it is believed that vCJD in humans results from the consumption of contaminated meat or meat by-products from BSE-infected cattle. Person-to-person transmission of kuru occurred through ritual practices involving cannibalism and no longer occurs in persons born after such practices were abandoned.

E. Incubation Period

The incubation period for iatrogenic CJD varies by route of exposure (15 months–30 years). The incubation period is unknown for sCJD and is believed to be variable for vCJD, with some cases having incubation periods as short as 5–10 years.

F. Period of Communicability or Infectious Period

CJD is not infectious in the usual sense; there is no evidence of person-to-person transmission by casual contact. The brain and other neurological tissues may be infectious when handled directly throughout symptomatic illness and possibly during the later stages of the incubation period.

G. Epidemiology

Kuru was first identified in the 1950s in Papua, New Guinea among individuals who participated in ritual mourning ceremonies involving cannibalism. It was determined that the chain of infection started early in the 20th century, possibly with ingestion of tissue from an individual with sCJD. The incidence of kuru declined following cessation of the ceremonies.

Sporadic CJD (sCJD) has been reported worldwide. The annual incidence rate for sCJD is approximately 1 case/1,000,000 population. The highest age-specific incidence rate (over 5 cases/1,000,000 population) occurs in those aged 65–79 years. CJD has been reported in persons aged 14–90 years, with over 95% of cases aged 35 years or older and with the peak of disease onset occurring in the 60–90 year-old age group. Familial CJD has an average age of onset that is approximately ten years younger than sCJD.

In 1996, a new form of CJD, denoted variant CJD (vCJD), was identified in the United Kingdom. The source of vCJD is thought to be cattle with BSE, on the basis of temporal association and some biochemical markers. Over 150 cases of vCJD have been reported worldwide, mainly from the United Kingdom. Variant CJD (vCJD) typically occurs at a younger age than CJD, with disease onset peaking in the 25–29 year-old age group and with a mean age at death of 28 years (range 12–74 years).

H. Bioterrorist Potential

This pathogen is not considered to be of risk for use in bioterrorism.

Section 2:

REPORTING CRITERIA AND LABORATORY TESTING

A. What to Report to the Massachusetts Department of Public Health (MDPH)

Report any of the following:

- A clinically-compatible case of CJD, as reported by a health care provider;
- A death certificate with CJD noted as the cause of death;
- Detection of 14-3-3 protein in cerebrospinal fluid (CSF) in a clinically compatible case;
- Neuropathological changes of spongiform nature, neuronal loss, astrocytosis, and amyloid plaque formation; or
- PrP immunocytochemistry and detection by Western blot, histoblot, and immunoblot techniques in a clinically compatible case.

B. Laboratory Testing Services Available

The MDPH State Laboratory Institute (SLI) does not provide laboratory services for diagnosing CJD.

Testing for the 14-3-3 protein marker is performed at private laboratories. The National Prion Disease Pathology Surveillance Center at Case Western Reserve University, at (216) 368-0587, can analyze CSF, blood, and brain tissue obtained either at biopsy or autopsy for prion diseases.

Brain tissue from rabies-negative cattle that presented with neurological disease is forwarded by the SLI to the National Veterinary Diagnostic Laboratory (NVDL) in Ames, Iowa, to rule out BSE.

For information on routine monitoring of cattle in Massachusetts for BSE, contact the Massachusetts Department of Agricultural Resources (MDAR), Division of Animal Health, Dairy Services, and Biosecurity (DAH) at (617) 626-1795.

Section 3:

REPORTING RESPONSIBILITIES AND CASE INVESTIGATION

A. Purpose of Surveillance and Reporting

- To monitor for the possible occurrence of vCJD in Massachusetts.
- To identify transmission sources of public health concern (e.g., food supply, biological pharmaceuticals, transplants, procedures).

B. Laboratory and Health Care Provider Reporting Requirements

CJD is reportable to the local board of health (LBOH). The MDPH requests that health care providers immediately report to the LBOH in the community where the case is diagnosed, all confirmed or suspect cases of CJD, as defined by the reporting criteria in Section 2A. This includes any suspect or confirmed cases of CJD <55 years of age because

suspect cases and deaths among persons with CJD <55 years of age are further investigated as possible vCJD cases. If it is not possible to contact the LBOH, please call the MDPH Division of Epidemiology and Immunization at (617) 983-6800 or (888) 658-2850.

Laboratories performing examinations on any specimens derived from Massachusetts residents that yield evidence of CJD infection shall report such evidence of infection directly to the MDPH within 24 hours.

C. Local Board of Health (LBOH) Reporting and Follow-up Responsibilities

MDPH regulations *(105 CMR 300.000)* stipulate that CJD is reportable to the LBOH and that each LBOH must report any case of CJD or suspect case of CJD, as defined by the reporting criteria in Section 2A.

Due to national surveillance and reporting requirements, the MDPH will take the lead on CJD investigation (including filling out the official case report form), in collaboration with the LBOH. The MDPH will keep the LBOH informed of all significant developments and will request the assistance of the LBOH as needed. Epidemiologists will contact the providers of patients with suspected CJD diagnoses and will complete a medical chart review.

Section 4:
CONTROLLING FURTHER SPREAD

A. Isolation and Quarantine Requirements *(105 CMR 300.200)*

None.

B. Protection of Contacts of a Case

None.

C. Managing Special Situations

Prevention of Iatrogenic CJD

Prion proteins cannot be inactivated by routine methods of decontamination. For any suspect cases of CJD for which a biopsy was performed, confirm with the infection control personnel that appropriate disinfection and sterilization methods were used on the neurosurgical instruments or devices as recommended by the Centers for Disease Control and Prevention (CDC). For more information, visit the CDC website, *Questions and Answers Regarding Creutzfeldt-Jakob Disease Infection-Control Practices*, at www.cdc.gov/ncidod/diseases/submenus/sub_bse.htm.

ADDITIONAL INFORMATION

The following is the formal National Creutzfeldt-Jakob Disease Surveillance Unit surveillance case definition for the various types of CJD. It is provided for your information only and should not affect the investigation and reporting of a case that fulfills the criteria in Section 2A of this chapter. For reporting to the MDPH, always use the criteria outlined in Section 2A.

Clinical Case Definition

Sporadic CJD (sCJD)

Suspect	◆ Rapidly progressive dementia **and** two of the following symptoms (myoclonus, visual or cerebellar problems, pyramidal or extrapyramidal features [e.g., motor dysfunction or Parkinsonian-like symptoms], or akinetic mutism [e.g., unmoving and unspeaking]) **and** duration of <2 years.
Probable	◆ Rapidly progressive dementia **and** two of the following symptoms (myoclonus, visual or cerebellar problems, pyramidal or extrapyramidal features [e.g., motor dysfunction or Parkinsonian-like symptoms], or akinetic mutism [e.g., unmoving and unspeaking]) **and** typical electroencephalogram (EEG). ◆ Suspect case + positive 14-3-3 CSF.
Confirmed	◆ Neuropathologically/immunocytochemically confirmed.

Iatrogenic CJD

Suspect	◆ Progressive predominant cerebellar syndrome in human pituitary hormone recipients. ◆ Probable CJD with recognized iatrogenic risk factor.*
Confirmed	◆ Confirmed CJD with recognized iatrogenic risk factor.*

* Relevant exposure risks for the classification as iatrogenic CJD:

- Treatment with human pituitary growth hormone, human pituitary gonadotrophin, or human dura mater graft.
- Corneal graft in which the corneal donor has been classified as confirmed or probable case of human prion disease.
- Exposure to neurosurgical instruments previously used in a case of definite or probable human prion disease.

  (Note: The relevance of any exposure to disease causation must take into account the timing of the exposure in relation to disease onset.)

Variant CJD (vCJD) (Refer to table below)

Suspect	◆ I **and** 4 out of 5 of II **and** III-A.
Probable	◆ I **and** 4 out of 5 of II **and** III-A **and** III-B. ◆ I **and** IV-A.[4]
Confirmed	◆ I-A and neuropathological confirmation of vCJD.[5]

I	A. Progressive neuropsychiatric disorder. B. Duration of illness >6 months. C. Routine investigations do not suggest an alternative diagnosis. D. No history of potential iatrogenic exposure. E. No evidence of familial form of TSE.
II	A. Early psychiatric symptoms.[1] B. Persistent painful sensory symptoms.[2] C. Ataxia. D. Myoclonus or chorea or dystonia. E. Dementia.
III	A. EEG does not show the typical appearance of sCJD[3] (or no EEG performed). B. Bilateral pulvinar high signal or MRI scan.
IV	A. Positive tonsil biopsy.[4]

1 Depression, anxiety, apathy, withdrawal, delusions.

2 This includes both frank pain and/or dysasthesia.

3 Generalized triphasic periodic complexes at approximately one per second.

4 Tonsil biopsy is not recommended routinely or in cases with EEG appearances typical of sCJD, but may be useful in suspect cases in which the clinical features are compatible with vCJD and MRI does not show bilateral pulvinar high signal.

5 Spongiform change and extensive PrP deposition with florid plaques, throughout the cerebrum and cerebellum.

REFERENCES

American Academy of Pediatrics. [Prion Diseases.] *Red Book: 2003 Report of the Committee on Infectious Diseases, 26th Edition*. Elk Grove Village, IL, Academy of Pediatrics; 2003: 510–512.

Belay, Ermias D. Transmissible Spongiform Encephalopathies in Humans. *Annual Review of Microbiology*. 1999; 53: 283–314.

"Bovine Spongiform Encephalopathy and Creutzfeldt-Jakob Disease." CDC/National Center for Infectious Diseases Website. June 29, 2005. <www.cdc.gov/ncidod/diseases/submenus/sub_bse.htm>.

Heymann, D.L., ed. *Control of Communicable Diseases Manual, 18th Edition.* Washington, DC, American Public Health Association, 2004.

MDPH. *Regulation 105 CMR 300.000: Reportable Diseases, Surveillance, and Isolation and Quarantine Requirements.* MDPH, Promulgated November 4, 2005.

Rutala, W.A., Weber D.J. Creutzfeldt-Jakob Disease: Recommendations for Disinfection and Sterilization. *Clinical Infectious Disease*. 2001; 32: 1348–1356.

"Creutzfeldt-Jakob Syndrome." World Health Organization. November, 2002. <www.who.int/topics/creutzfeldtjakob_syndrome/en>.

FORMS & WORKSHEETS

Prion Disease

(Also known as Transmissible Spongiform Encephalopathies [TSEs]; includes Creutzfeldt-Jakob Disease [CJD], Gerstmann-Straussler-Scheinker Disease [GSS], Fatal Familial Insomnia [FFI], Kuru, and Variant CJD [vCJD])

Prion Diseases

(Also known as Transmissible Spongiform Encephalopathies [TSEs]; includes Creutzfeldt-Jakob Disease [CJD], Gerstmann-Straussler-Scheinker Disease [GSS], Fatal Familial Insomnia [FFI], Kuru, and Variant CJD [vCJD])

LBOH Action Steps

This form does not need to be submitted to MDPH with the case report form. It is for LBOH use and is meant as a quick-reference guide for CJD case investigation activities.

LBOH staff should follow these steps when CJD is suspected or confirmed. For more detailed information, including disease epidemiology, reporting, case investigation, and follow-up, refer to the preceding chapter.

Note: Due to national surveillance and reporting requirements, MDPH will lead CJD investigations (including filling out the official case report form), in collaboration with the LBOH. MDPH epidemiologists will keep the LBOH informed of all significant developments and will request the assistance of LBOH as needed.

- ❑ Notify the MDPH Division of Epidemiology and Immunization, at (617) 983-6800 or (888) 658-2850, to report any confirmed or suspect case(s) of CJD.
- ❑ If requested, and in collaboration with MDPH, fill out the case report form (attach laboratory results).
- ❑ If requested, send the completed case report form (or portions completed), with laboratory results, to the MDPH Bureau of Communicable Disease Control, Office of Integrated Surveillance and Informatics Services (ISIS).